

# PATENT COOPERATION TREATY

# PCT

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## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 21729		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/EP2004/003739		International filing date (day/month/year) 07.04.2004	Priority date (day/month/year) 10.04.2003	
International Patent Classification (IPC) or national classification and IPC C12Q1/34, C07K16/40, C12N9/16, A61K31/00, A61K38/00, A61K39/00, A61P9/00				
Applicant F. HOFFMANN-LA ROCHE AG et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  28.09.2004		Date of completion of this report  21.03.2005		
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Döpfer, K-P  Telephone No. +49 89 2399-8547		



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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-17 as originally filed

**Sequence listings part of the description, Pages**

18-39 as originally filed

**Claims, Numbers**

1-20 as originally filed

**Drawings, Sheets**

1-11 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 20

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 20

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-15,19
	No: Claims	16-18
Inventive step (IS)	Yes: Claims	
	No: Claims	1-19
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	

**2. Citations and explanations (Rule 70.7):**

**see separate sheet**

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**Box No. VI Certain documents cited**

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**1. Certain published documents (Rule 70.10)**

and / or

**2. Non-written disclosures (Rule 70.9)**

**see separate sheet**

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**Supplemental Box relating to Sequence Listing**

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**Continuation of Box I, item 2:**

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
  - a. type of material:
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing:
    - ☒ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
    - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

**Re Item I**

**Basis of the report**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. No International Search Report has been drawn up for the subject-matter of present claim 20. According to Rule 66(1)(e) PCT no International Preliminary Examination is being carried out for the subject-matter of these claims.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following documents:
  - D1: WO 2004/042389 A (BAYER HEALTHCARE AG ; GOLZ STEFAN (DE); GEERTS ANDREAS (DE); BRUEGGEME) 21 May 2004 (2004-05-21); see item VI of this written opinion
  - D2: WO 01/57036 A (MARFAT ANTHONY ; PFIZER PROD INC (US); CHAMBER ROBERT JAMES (US)) 9 August 2001 (2001-08-09)
  - D3: ISMAIL F M D: "Important fluorinated drugs in experimental and clinical use" JOURNAL OF FLUORINE CHEMISTRY, ELSEVIER SEQUOIA, LAUSANNE, CH, vol. 118, no. 1-2, 1 December 2002 (2002-12-01), pages 27-33, XP004393604 ISSN: 0022-1139
  - D4: WO 02/074992 A (DECODE GENETICS EHF ; GRETARSDOTTIR SOLVEIG (IS); JONSDOTTIR SIF (IS);) 26 September 2002 (2002-09-26)

2. Novelty and Inventive Step (Article 33(2)(3) PCT)

- 2.1 The present application addresses methods of screening for medicaments against atherosclerosis or restenosis using PDE4D isoforms, compounds for therapy of atherosclerosis or restenosis (identified by the screening methods), pharmaceutical compositions comprising these compounds, and the use of these compounds for the preparation of medicaments for the treatment of atherosclerosis or restenosis.
- 2.2 None of the cited prior art documents discloses the use of PDE4D isoenzymes for the identification of compounds for the therapy of atherosclerosis or restenosis. Accordingly, present claims 1-15 are novel over the prior art.

Present claim 16 is directed to any compound per se which inhibit PED4D isoforms. It is drafted as a so-called "reach-through" claim, i.e. any compound, known or unknown, with the desired activity is claimed.

Inhibitors of PED4D are known from the disclosure of D2 to D4. These compounds fall within the scope of present claim 16. Claims 17 and 18 pertain to pharmaceutical compositions and second medical uses of the compounds of claim 16. These compositions and uses are not novel either in the light of the prior art documents cited. The use for POAD appears to be not inventive in the view of the known uses.

D4 is regarded as representing the closest prior art. It addresses the role of the human PDE4D gene in stroke. This document deals also with the involvement of PDE4D expression in ischemic stroke. Ischemic stroke is mainly caused by occlusive incidents in the brain vasculature. This can be seen as an indirect hint to atherosclerosis (restenosis is not contemplated at all). But the document is silent with respect to the treatment of atherosclerosis as a systemic disease dependent upon the activity of PDE4D isoforms in e.g. intimate cells of blood vessels. The problem underlying the present application can be seen as to provide further therapeutic applications of PDE4D inhibitors. If atherosclerosis is dependent on PDE4D isoform activity, any PDE4D inhibitor would also be suitable as medicament for the therapy of atherosclerosis. D4 describes in general screening methods for identifying inhibitors of PDE4D isoforms. The skilled person would apply this methodology to the posed problem, i.e. the subject-matter of present claims 1-15 does not involve an inventive step in view of the closest prior art.

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(SEPARATE SHEET)**

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**Re Item VI**

**Certain documents cited**

**Certain published documents**

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-A-2004042389	21/05/2004	25/10/2003	08/11/2002

The subject-matter of the entire document WO-A-2004042389 (D1) is considered pertinent for the novelty of present claims 1-19 when entering the regional phase under the EPC.

**Re Item VIII**

**Certain observations on the international application**

1. Claim 20 is not directed to a well defined category, i.e. it is directed to compounds, processes, uses and compositions. Furthermore it does not contain technical features which characterise the subject-matter for which protection is sought. So this claim lacks clarity in the sense of Article 6 PCT to such an extent that neither a meaningful search nor an examination is possible.